

REMARKS

Applicants submit these remarks and amendments in response to the Office Action dated July 15, 2003. The specification has been amended to clarify the Figure legends, as requested by the Examiner. Claim 23 is amended as discussed below in response to the new matter rejection. Claim 24 is amended to be consistent with the response to the Restriction Requirement.

New claims 33-37 are added to claim specific embodiments of the invention. Claim 33 is supported at least at page 6, lines 11-21; claim 34 is supported at least at page 6, lines 11-15; claim 35 is supported at least at page 2, lines 5-6 and 9-10, and at page 10, lines 9-12 and 15; claim 36 is supported at least at page 10, lines 9-12 and 15, and page 6, lines 11-18; and claim 37 is supported at least at page 10, lines 9-12 and 15, and page 6, lines 11-18. Claims 1-22 were previously cancelled; and claims 26, and 28-32 are withdrawn. Claims 25 and 27 remain pending.

In the Office Action, the Examiner stated that claim 25 is free of the prior art, and claim 27 was examined based on its inclusion in the prior art cited by the Examiner in the search of the elected invention. In view of this, claim 23 is amended to recite both stroke and Parkinson's disease, as the corresponding dependent claims (25 and 27) have been examined on the merits.

The issues raised in the Office Action are addressed below in paragraphs numbered to correspond to the paragraphs in the Office Action.

1. The specification has been amended at page 38, to refer to the sequence by as SEQ ID NO:6.
2. Applicants note the Examiner's statement that a certified copy of the foreign priority application has not been filed. This application (Serial No. 09/836,960) claims priority back to provisional U.S. application 60/083,553, April 29, 1998. There is no earlier foreign priority document from which to provide a certified copy. This ground of rejection is moot.
3. The Examiner states that applicants have not complied with one or more conditions for receiving the benefit of an earlier filing date. Specifically, the Examiner states that support is not found for "A method for providing trophic support ... comprising administration to neuronal cells..." as claimed, and that the provisional applications lack the disclosure of Examples 6 and 7. The Examiner further notes that the effective filing date of the present claims is indicated to be March 8, 1999, the date of filing of application Serial No.

09/264,851. Applicants acknowledge the Examiner's comments. Claim 23 has been amended and no longer recites "trophic support" language.

4. The drawings were objected to because the specification allegedly did not reference certain figures in the required format. This has been corrected by amendment of the Figure legends. The Examiner noted that the labels on Figure 5 appear to indicate that fractions 23-24 show a single band, instead of fractions 22-23. In addition, Figure 11 references Panels A and B, but these are not labeled on the figure. Corrected Figure 11 is filed herewith, and the description of Figure 5 has been amended.

5. Applicants acknowledge the claims under examination as a result of the restriction requirement.

6-7. Claims 23-25 and 27 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement, as a new matter issue. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

The Examiner stated that support was not found for "a method for providing trophic support for cells ex vivo comprising administering to neuronal cells from a patient suffering from a condition capable of treatment with a neurotrophic factor a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4." Applicants submit that the Examiner is focusing on very specific nuances of language, and in fact the support does exist, for example at page 6, lines 11-21. However, in order to advance the prosecution of the application, claim 23 has been amended to reflect language found literally in the specification, for example, at page 6, lines 11-21. Growth of cells of the nervous system is supported at page 6, line 13; and Example 6 at page 36. Survival of cells of the nervous system is supported at page 6, lines 14-15, and Example 3, pages 32-33.

8. Claims 23-25 and 27 are rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly is not enabled for trophic support for cells ex vivo as generically claimed, or for providing such activity in neuronal cells from a patient suffering from a condition capable of treatment with a neurotrophic factor as claimed.

Regarding the "ex vivo" language, the Examiner states that the recitation is in generic form in view of the preamble recitation. Applicants have amended claim 23 to reflect the intended embodiment of support for neuronal cells. Regarding the support to cells from a patient

suffering from any of the enumerated disease conditions, applicants note first that the claims have been amended to reflect the election of Parkinson's disease, and that stroke is also included in view of the Examiner's statement as noted above in the introductory remarks.

The Examiner cites two publications, Florenes et al., *Cancer Res.* 54:354-356 (1994) and Zimmerman et al., *Neuron* 12:11-24 (1994) which allegedly teach differences between neural progenitor cells and neurons, as exemplified by nestin expression in proliferating neural stem cells, down-regulation in postmitotic neurons, and an absence of expression in adult brain. The Examiner states that nestin-positive stem cell precursors do not necessarily develop into neurons, but are "hallmarks" of cancer cells, myocytes, and neuroepithelial cells. In addition to the two publications above, the Examiner also cites Gallo et al., *J. Neuroscience* 15:394-406 (1995), and concludes that the increased proliferation of cells as measured by Nestin expression (Examples 6 and 7) does not appear to be "particular" to neuronal cells as claimed.

Finally, the Examiner states that Hoshikawa et al., *Br. Res. Mol. Br. Res.* 105:60-66 (2002) reported that FGF-18 was not observed to exhibit neurotrophic activity in cultured rat cortical neurons. Without acquiescing to the grounds of rejection, applicants submit that the claims as amended are not subject to this rejection.

9. Claims 23-25 and 27 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter of the invention. The Examiner states that the specification provides no guidance as to the metes and bounds of the term "trophic support." The Examiner cites Jessel et al., *Neuronal Survival and Synapse Formation*, in *Principles of Neural Science*, Third Ed., Kandel et al., Elsevier, 1991, page 292, to support the distinction between trophic factors that are essential to the survival of neurons, and growth factors that support cell division but are not required for survival. As discussed above, claim 23 no longer recites the term "trophic support," so this ground of rejection may be withdrawn.

The Examiner further notes that the term "ex vivo" is not clear because the method fails to note removal of cells from the patient. This has been addressed by the amendment of claim 23 herein. Reconsideration and withdrawal of this rejection are respectfully requested.

11-12. Claims 23-24 and 27 are rejected under 35 U.S.C. § 102(a) and (e) as being allegedly anticipated by Deisher et al., U.S. Patent No. 5,989,866, filed October 16, 1997 and

issued November 23, 1999. The Examiner basis this rejection on an effective filing date of the current claims as March 8, 1999. The reference teaches zFGF-5, which according to the Examiner is 100% identical to SEQ ID NO:5, and encoded by SEQ ID NO:4, of the present application, and methods of using the polypeptide. Reconsideration and withdrawal of this ground of rejection are respectfully requested.

Applicants have amended claim 23 to clarify that the cells treated are precursor cells of the nervous system. In the context of the present rejection, the Examiner stated that the preamble of claim 23 is deemed to include trophic support for bone and myocytes. With the amendment to claim 23, application submit that the Deisher patent is not prior art to the invention as claimed.

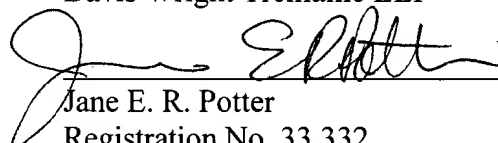
All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

If questions remain regarding this application, the Examiner is invited to contact the undersigned at (206) 628-7650.

Respectfully submitted,

Hui Cen et al.

Davis Wright Tremaine LLP



Jane E. R. Potter
Registration No. 33,332

2600 Century Square
1501 Fourth Avenue
Seattle, WA 98101-1688
Phone: (206) 622-7650
Fax: (206) 628-7699